

What is Claimed is:

1. An immunostimulatory combination comprising:  
a TLR agonist and a TNF/R agonist, each in an amount that, in combination with the other, is effective to increase a subject's immune response to an antigen.
- 5 2. The immunostimulatory combination of claim 1 wherein the TLR agonist is an agonist of at least one of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, or any combination of any of the foregoing.
- 10 3. The immunostimulatory combination of claim 2 wherein the TLR agonist comprises an IRM compound or an agonist of TLR2.
- 15 4. The immunostimulatory combination of claim 1 wherein the TLR agonist comprises an IRM compound, MALP-2, LPS, polyIC, CpG, or any combination of any of the foregoing.
- 20 5. The immunostimulatory combination of claim 3 wherein the IRM compound comprises an imidazoquinoline amine, a tetrahydroimidazoquinoline amine, an imidazopyridine amine, a 1,2-bridged imidazoquinoline amine, a 6,7-fused cycloalkylimidazopyridine amine, an imidazonaphthyridine amine, a tetrahydroimidazonaphthyridine amine, an oxazoloquinoline amine, a thiazoloquinoline amine, an oxazolopyridine amine, a thiazolopyridine amine, an oxazolonaphthyridine amine, or a thiazolonaphthyridine amine.
- 25 6. The immunostimulatory combination of claim 1 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.
- 30 7. The immunostimulatory combination of claim 6 wherein the TNF/R agonist comprises an agonist of CD40 ligand, OX40 ligand, 4-1BB ligand, CD27, CD30 ligand (CD153), TNF- $\alpha$ , TNF- $\beta$ , RANK ligand, LT- $\alpha$ , LT- $\beta$ , GITR ligand, or LIGHT
8. The immunostimulatory combination of claim 1 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.

9. The immunostimulatory combination of claim 8 wherein the TNF/R agonist comprises an agonist of CD40, OX40, 4-1BB, CD70 (CD27 ligand), CD30, TNFR2, RANK, LT- $\beta$ R, HVEM, GITR, TROY, or RELT.

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10. The immunostimulatory combination of claim 1 wherein the TNF/R agonist comprises an agonistic antibody.

10 11. A method of inducing a T<sub>H</sub>1 immune response in a subject comprising:  
co-administering to the subject a TLR agonist and a TNF/R agonist, each in an amount that, when in combination with the other, is effective to induce a T<sub>H</sub>1 immune response.

15 12. The method of claim 11 wherein the TLR agonist comprises an agonist of TLR2.

13. The method of claim 11 wherein the TLR agonist comprises an agonist of TLR9.

20 14. The method of claim 11 wherein the TLR agonist comprises an agonist of TLR8.

25 15. The method of claim 11 wherein the TLR agonist comprises an agonist of TLR7.

16. The method of claim 11 further comprising co-administering an antigen in an amount effective to induce an immune response in the subject.

30 17. A method of activating antigen-specific CD8<sup>+</sup> T cells in a subject comprising:  
co-administering to the subject a TLR agonist and a TNF/R agonist, each in an amount that, in combination with the other, is effective to activate antigen-specific CD8<sup>+</sup> T cells.

18. The method of claim 17 further comprising co-administering an antigen in an amount effective to induce an immune response in the subject.

5 19. The method of claim 17 wherein activating CD8<sup>+</sup> T cells comprises expansion of CD8<sup>+</sup> effector T cells.

20. The method of claim 17 wherein activating CD8<sup>+</sup> T cells comprises generating CD8<sup>+</sup> memory T cells.

10 21. The method of claim 17 wherein the TLR agonist comprises an agonist of TLR2.

22. The method of claim 17 wherein the TLR agonist comprises an agonist of TLR9.

15 23. The method of claim 17 wherein the TLR agonist comprises an agonist of TLR8.

20 24. The method of claim 17 wherein the TLR agonist comprises an agonist of TLR7.

25. The method of claim 17 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.

25 26. The method of claim 17 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.

27. The method of claim 17 wherein the TNF/R agonist comprises an agonistic antibody.

30 28. A method of activating antigen-specific memory CD8<sup>+</sup> T cells in a subject having prior exposure to an antigen, comprising:

administering to the subject the antigen in an amount effective to induce antigen-specific CD8<sup>+</sup> memory T cells to become activated, thereby generating antigen-specific CD8<sup>+</sup> effector T cells.

5        29.     The method of claim 28 further comprising co-administering a TLR agonist in an amount effective to induce antigen-specific CD8<sup>+</sup> memory T cells to become activated, thereby generating antigen-specific CD8<sup>+</sup> effector T cells.

10       30.     The method of claim 28 wherein the TLR agonist comprises an agonist of TLR2.

31.     The method of claim 28 wherein the TLR agonist comprises an agonist of TLR9.

15       32.     The method of claim 28 wherein the TLR agonist comprises an agonist of TLR8.

20       33.     The method of claim 28 wherein the TLR agonist comprises an agonist of TLR7.

34.     A method of treating a condition in a subject comprising:  
co-administering to the subject a TLR agonist and a TNF/R agonist, each administered in an amount that, when in combination with the other, is effective for stimulating a cell-mediated immune response.

25       35.     The method of claim 34 wherein the TLR agonist comprises an agonist of TLR2.

30       36.     The method of claim 34 wherein the TLR agonist comprises an agonist of TLR9.

37.     The method of claim 34 wherein the TLR agonist comprises an agonist of TLR8.

38. The method of claim 34 wherein the TLR agonist comprises an agonist of TLR7.

5 39. The method of claim 34 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.

40. The method of claim 34 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.

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41. The method of claim 34 wherein the TNF/R agonist comprises an agonistic antibody.

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42. The method of claim 34 further comprising co-administering an antigen associated with the condition in an amount effective for inducing a cell-mediated immune response.

43. The method of claim 34 wherein the condition comprises a neoplastic disease.

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44. The method of claim 43 wherein co-administering the TLR agonist and the TNF/R agonist provides prophylactic treatment.

45. The method of claim 43 wherein co-administering the TLR agonist and the TNF/R agonist provides therapeutic treatment.

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46. The method of claim 34 wherein the condition comprises an infectious disease.

47. The method of claim 46 wherein co-administering the TLR agonist and the TNF/R agonist provides prophylactic treatment.

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48. The method of claim 46 wherein co-administering the TLR agonist and the TNF/R agonist provides therapeutic treatment.

49. A vaccine comprising:

a TLR agonist, a TNF/R agonist, and an antigen, each in an amount that, in combination with the others, is effective for inducing an immune response to the antigen in a subject immunized with the vaccine.

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50. The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR2.

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51. The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR9.

52. The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR8.

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53. The vaccine of claim 49 wherein the TLR agonist comprises an agonist of TLR7.

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54. The vaccine of claim 49 wherein the TNF/R agonist comprises an agonist of a TNF Superfamily member.

55. The vaccine of claim 49 wherein the TNF/R agonist comprises an agonist of a TNFR Superfamily member.

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56. The vaccine of claim 49 wherein the TNF/R agonist comprises an agonistic antibody.

57. The vaccine of claim 49 wherein the antigen comprises a tumor antigen, a viral antigen, a bacterial antigen, or a parasitic antigen.

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